REMARKS

Claims 1-10 and 12-33 are pending in the application. Claims 14-22 and 30-32 are withdrawn from further consideration without prejudice. Claims 1 and 23 have been amended to recite the phrase "wherein the second population of cells substantially comprises cells of a different cell type than the first population" can be found throughout the specification and claims are originally filed, and specifically at page 3, lines 30-33 and page 7, line 11. Claims 3, 4, 12, and 27 have been amended to clarify the claimed invention. Claims 5 and 13 have been cancelled. No new matter has been added.

Amendment of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and has been done solely to more particularly point out and distinctly claim the invention, to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Claim Objections

Claim 13 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 13 has been cancelled rendering this rejection moot.

Rejection of Claims 1-10 and 12-13 under 35 U.S.C. 112 second paragraph

Claim 1-10, and 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office Action states that "claim 1 is confusing as written, particularly with regards to the phrase, 'a VEGF angiogenesis modulating agent'." Claim 1 has been amended to recite the language suggested by the Examiner. Accordingly, the Examiner is requested to withdraw this rejection.

Rejection of Claims 1, 3, 12, and 13 under 35 U.S.C. 102(e)

Claims 1, 3, 12, and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Penn et al (US 2004/0161412 A1) as supported by provisional applications 60/424,065 and 60/405,274. Applicants traverse this rejection.

Independent claim 1, (and dependent claims 3 and 12) has been amended to recite the step of "co-administering a second population of cells, wherein the second population of cells substantially comprises cells of a *different cell type* than the first population." Penn *et al.* do not disclose the implantation two cell populations comprising *two different cell types* as admitted by the Examiner (See page 5-6 of the Office Action where the Examiner points out that the two different cell populations in Penn *et al.* refer to the "successfully transiently transfected cells and non-transfected cells"). Accordingly, Penn *et al.* fails to anticipate the claimed invention.

Since Penn *et al.* do not disclose each and every limitation of claims 1, 3, and 12, the Examiner is respectfully requested to withdraw this rejection. Claim 13 has been canceled rendering the rejection of this claim moot.

Rejection of Claims 1-10, 12-13, 23-29 and 33 are rejected under 35 U.S.C. 103(a)

Claims 1-10, 12-13, 23-29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala *et al.* (US Patent 6,479,064), in view of Penn et al (US 2004/0161412 A1) further in view of Cima *et al.* (J. Biomed Engineering, 1991) and Griffith-Cima (US Patent 5,709,854). Claims 5 and 13 have been canceled. Applicants traverse the rejection of claims 1-4, 6-10, 12, 23-29 and 33.

As amended, independent claim 1 (and claims 2-4, 6-10, 12 dependent thereto) recite the step of "co-administering a second population of cells, wherein the second population of cells substantially comprises cells of a *different cell type* than the first population" Independent claim 23 (and claims 24-29, and 33 dependent thereto) recite that "the second population of cells substantially comprises cells of a *different cell type* than the first population."

The Office Action states that the Atala reference is "relatively general on the types of cell that can be used." Penn *et al.* does not remedy this deficiency since Penn *et al.* does not teach or even suggest co-implanting *two different cell types*. For example, the Examiner states that while "Penn et al teach transfecting a population of myoblasts, it will be understood that both successfully transiently cells and non-transfected cells will be injected (which applicant calls two separate populations of myoblasts)." Accordingly, the two populations of cells taught in the Penn reference are the same type of cells (i.e., myoblasts). In contrast, the amended independent claims (and claims dependent thereto) require *two different cell types*.

Further the Office Action states that:

> it also would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use three-dimensional matrices made from polymers such as polylactic acids or polyglycolic acids or combinations thereof (PLAs, PGAs, or PLGAs), such as those described by Cima *et al.*

Also that:

> Griffith-Cima at al provide another alternative to decellularized tissue in US Patent 5,709,854, where they disclose a matrix comprised of hydrogel, in which cells can be cultured and then subsequently injected into a patient to form an organ equivalent or tissue construct (See col. 1, In 27-58).

Applicants respectfully traverse the rejection. The invention relates to organ enhancing, e.g,, improving the function of an organ that is operating at less than optimum capacity. The claimed invention achieves organ augmentation by transiently transfecting cells to express the angiogenesis modulating agent VEGF. The expressed factor induces assimilation and differentiation of cells at the target site. This gain in function results in an organ that is operating at a physiologically acceptable capacity for that subject. This is accomplished by injecting encapsulated cells transiently transfected with VEGF into a target site together with a *second*

population of cells of a different cell type, such that the VEGF induces assimilation and differentiation of the cells at the target region.

Atala *et al.* describes how to prepare artificial organ constructs from decellularized scaffold matrices seeded with endothelial cells. These endothelial cells produce a vascular system that supports the growth of other cell populations. Atala *et al.* teach that these constructs can be made by using a decellularized biostructure of an "organ, or part of an organ" (Column 5, lines 34-35). Atala *et al.* also teaches decellularizing of an entire kidney and then using the kidney scaffold as a matrix for cell population. The entire cell seeded scaffold is then transplanted into a host (Example 6, column 19). Thus, the entire teaching of Atala *et al.* is for using tissue engineered implants that *replace* organs. To the extent that Atala *et al.* speaks of augmenting the tissue function, it is only in the context of *replacing* the organ or part of the organ with a cell seeded matrix.

Furthermore, there is no teaching or suggestion of organ augmentation by implanting *transiently* transfected cells that express the VEGF angiogenesis modulating agent. Thus, Atala *et al.* fail to teach or suggest the claimed invention.

Cima *et al.* only provides a general discussion for restorable matrices made from polymers such as polylactic acids or polyglycolic acids or combinations thereof (PLAs, PGAs, or PLGAs). There is no teaching or suggestion in Cima *et al.* for expressing the angiogenesis modulating agent VEGF to augmenting organ function, nor the use of two different cell types.

Griffith-Cima only provides a general discussion for suspending cells in hydrogels. There is no teaching or suggestion for transiently expressing the angiogenesis modulating agent VEGF in one population of cells, and co-administrating a second population of cells of a *different cell type*, as recited by the claimed invention.

For all the forgoing reasons, the references alone, or in combination fail to arrive at the claimed invention. Accordingly, the Examiner is respectively requested to withdraw the obviousness rejection over claims 1-4, 6-10, 12, 23-29 and 33.

Double Patenting

Claims 1, 5, 8, 10, 23-26 and 29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11, 16, 17 and 18 of co-pending Application No. 10/292,166 (co-pending application '166) . Applicants traverse this rejection.

The rejected claims do not comprise an obvious variation of co-pending application '166. Specifically, there is not even a teaching or a suggestion of the need to *transfect* cells with a plasmid encoding the angiogenesis modulating agent VEGF, much less the need for *transient* transfection of the cells. The present invention clearly teaches how to transfect cells in a *transient* manner such that the transfected cells, once delivered to the target site, are able to express the angiogenesis modulating agent (e.g., VEGF) for a limited period of time to increase the angiogenesis modulating agent at a localized region. After such period of time, the cellular production of VEGF is diminished due to the transient nature of the transfection. As a result, the amount of VEGF decreases over time without reaching toxic levels. Thus, the amount and time of VEGF release is controlled to induce assimilation and differentiation of cells in the target region to allow augmentation of organ function, but not to cause an adverse toxic effect. Furthermore, as amended, claims 1, 5, 8, 10, 23-26 and 29 recite that the first population of cells are *transiently* transfected while a second population of cells is co-administered. There is no teaching or suggestion in the co-pending application '166 to suggest the *transiently* transfection of one cell population together with the co-administration of a second population of cells of a different type. Without any suggestion or motivation in the co-pending application, it is improper to reconstruct the patentee's claimed invention by using the patentee's claim as a blueprint. Accordingly, the Examiner is respectfully requested to withdraw the rejection.

CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. In the event that the amendments and remarks are not deemed to overcome the grounds for rejection, the Examiner is kindly requested to telephone the undersigned representative to discuss any remaining issues.

Respectfully submitted,

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Date: March 20, 2006

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